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From Myth to Truth: Magnesium supplementation in athletes

Do Mito à Verdade: Suplementação de Magnésio em atletas

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Numa sociedade em que o acesso à informação não evoluiu no mesmo sentido da qualidade de mesma, percebemos que atualmente não interessa a credibilidade quando toca a divulgar informação sobre variadíssimos temas. De uma forma mais específica, quando falamos de suplementos alimentares, não interessa fornecer o melhor produto, com provas dadas da sua eficácia, mas apenas importa vender. Todos estes fatores acabam por contribuir para uma dissonância cognitiva, em que, apesar da informação estar mais acessível a todos, a probabilidade de estarmos desinformados acerca de algum tema é elevada.

No que toca à comercialização de suplementos alimentares, podemos encontrar uma variedade infinita de artigos. Dentro deste miríade de produtos, o Magnésio é um dos suplementos minerais mais tomados por desportistas.

O objetivo desta monografia é colocar um ponto final nos mitos que rodeiam a suplementação de magnésio em atletas, através de uma revisão detalhada de vários artigos científicos relacionados com o tema.

In a society in which access to information did not evolve in the same sense of its quality, we realize that credibility is not currently relevant when it comes to disseminating information on a wide range of subjects. More specifically, when it comes to food supplements, it does not matter to provide the best product with proven efficacy, but it's all about selling. All these factors end up contributing to a cognitive dissonance, in which, although the information is more accessible to all, the probability of being uninformed about some subject is high.

As far as the marketing of food supplements, we can find an infinite variety of articles. Within this myriad of products, Magnesium is one of the mineral supplements most taken by athletes.

The objective of this monograph is to put an end to the myths surrounding magnesium supplementation in athletes, through a detailed review of several scientific articles related to the subject.

Magnésio, suplementação, performance física

Magnesium, suplementation, physical performance

Lista de abreviaturas, siglas e acrónimos

Magnesium – Mg

Recommended daily allowance – RDA

Randomized controlled trial - RCT

Index

RESUMO I

INTRODUCTION 1

MAGNESIUM INTAKE 2

METHODS TO EVALUATE MAGNESIUM STATUS 5

ERGOGENIC THEORY 6

SCIENTIFIC EVIDENCE 9

DISCUSSION & CONCLUSION 13

AGRADECIMENTOS 15

REFERENCES 16

Introduction

Magnesium (Mg) is an essential element in the human organism, it is the fourth most abundant cation in our body, the second most common intracellular cation and the most common intracellular divalent cation[1]. It plays a key role in more than 300 enzymes in the human body[2].

We contain over 25 g of Mg in our body and our serum concentrations range between 75 to 95 mmol/L in heathy individuals[3].

Our organism stores almost 99% of Mg in bone, muscles and non-muscular soft tissue[4]. Extracellular represents only 1% of the total body Mg[4], and can be found primarily in serum and red blood cells[5]. The main functions that Mg takes part include mitochondrial oxidative phosphorylation, ionic balance maintenance, cellular and tissue integrity, glycolysis and DNA, RNA and protein synthesis and integrity[6]. In order to maintain our constant Mg plasma levels, the daily recommendation allowance is 420 mg for men and 320 mg for women[7].

Mg homeostasis depends on the combined work of the intestine, which is responsible for its uptake from our diet, the bone, responsible for its stocks, and the kidneys, that regulate the urinary excretion[8]. To maintain Mg concentrations the bone is in constant exchange with blood, thus, Mg deficiency results in decreased bone formation[9].

In theory, it is possible to use Mg as an ergogenic aid due to its role in energy production and storage, normal muscle function and maintenance of blood glucose levels. This monography will try to end the myths that surround the supplementation

of Mg in athletes by analysing past date articles and compare them with recent ones, in order to clarify this subject.

Magnesium intake

As previous said, Mg recommended daily allowance (RDA) is 420 mg for men and 320 mg for women. Mg deficiency is not only determined by its intake but also by the proportions of other nutrients and anti-nutrients in our intestine that will affect its bioavailability[2, 10].The process of Mg absorption is influenced by the high intake of other minerals like calcium, phosphorous, iron, copper, aluminium and manganese[11]. Also throughout the decades we have been witnessing a mass reduction of Mg concentrations in our daily food, either for over-processed food or the fertilisation of agriculture soils that manages to reduce Mg content in plant products[12]. There is even an article that states “Magnesium deficiency in plants is becoming an increasingly severe problem with the development of industry and agriculture and the increase in human population”[13]. There has been some controversy if requirements to achieve Mg positive balance are increased when a diet is rich in calcium, since there are some studies that proclaimed that a calcium intake over 10 mg/kg/day would affect the absorption of Mg[14, 15]. Despite this, a more recent article contradicts and proves wrong previous studies in these matter[16], stating that “Specifically, Mg bioavailability was not influenced by the presence of SO_4^{2-}, HCO_3^-, or calcium”. Phytic acid, present in seeds, nuts, and grains such as wholemeal bread very popular among athletes[17], can also diminish the gut absorption of Mg.

Some sports that require weight control like martial arts related (mixed martial arts, judo, taekwondo, etc) are well known for the use of diuretics by its practitioners, and the use of these medications can lead to Mg deficiency[2].

The richest foods in Mg content are almonds, bananas, nuts, seeds, egg yolk, fish oil, beans, broccoli, milk, soy beans, green leafy vegetables and whole grains, although this only leads up to a rough 10% of the recommended intake of Mg[18] which may open a door to supplementation or to other types of sources of Mg.

If there are ways to reduce Mg absorption, there are also ways to improve it, such as a high intake of vitamin D[19] and a more promising method to maintain positive balance of Mg is the use of a specific types of mineral water.

Epidemiological Magnesium deficiency

Hypomagnesemia can result in disturbances in nearly every organ system and cause potentially fatal complications (eg, ventricular arrhythmia, coronary artery vasospasm, sudden death). The first clinical signs are usually absent. After some time with very low intake of Mg the neuromuscular system stars to fail (weakness; tremor; Muscle fasciculation; dysphagia; spasms), the following systems to be affected is the cardiac structure (arrhythmias and ECG changes) and the central nervous system (depression; agitation; pshycosis)[17].

Reports of low intake of Mg are very frequent, with an estimated average of 56% of the population in the USA with inadequate intakes of Mg[20]. It has been found that the probability of an inadequate Mg intake on University students is 70% for women and 94% for men[21].

It's a well-known fact that for an optimal performance in any sport there must be a careful connection between nutrition and training. The better the diet the better the performance. The lack of any nutrient or micronutrient may lead to a decline in the athletic performance of the athlete. In particular, Mg deficiency has been associated with strength and power loss as well as reduced endurance work performance[22, 23].

Mg deficiency is no strange to athletes, since it was found, in young elite German female football players that 22% of the players did not meet the RDA for Mg. Likewise, a study done in weightlifters reported that during the "cut phase" for the weight control in the Olympics, the intakes of Mg were significantly low compared to the recommendations[24].

Maria Silva & Hugo Silva reported in rink hockey players (n=72 RH and n=79 controls) a very low intake of Mg (μ = 210 mg/day)[25]. The authors documented energy and nutrient intake from a 3-day dietary record, compromising 2 days of training and weekend's day. The reports showed a low intake of important vitamins and minerals, including Mg.

Teixeira et al. evaluated dietary intakes in Portuguese Professional referees (n = 83). The participants were asked to record everything they drank and ate for a period of 7 days and the results showed that 26% of the participants did not achieve the recommended intakes of Mg [26].

Since Mg deficiency has been associated to lower bone density, Matias et al. [27] studied if Mg ingestion could influence bone mineral density and lean soft tissue in elite male (n = 8) and female (n = 9) swimmers. They measured the subjects body composition and bone mineral density using a dual energy X-ray absorptiometry and in order to evaluate their Mg intake it was used a 7-day food record. In sequence of

this, it was reported a substantial lower intake of Mg. It was also reported a strong association concerning bone mineral density and lean soft tissue. After the increase in Mg in the athletes diet, they reported it has a strong predictor of bone density. Matias et al. stated that, young athletes that practiced low–impact sports, should be more aware of the association between Mg and bone mineral density during their growth.

Methods to evaluate magnesium status

The most common method to evaluate Mg levels is by examining serum Mg. Nevertheless, there has been a lot of discussion if this is the best way to assess Mg status.

The issue of measuring Mg status through serum Mg is the lag time between the serum changes and in Mg subclinical deficiency[28]. In other words, the serum concentrations do not become obvious if there is a deficiency of this mineral or not. It has been stated “The magnesium content of the plasma is an unreliable guide to body stores: muscle is a more accurate guide to the body content of this intracellular cation”[3]. Has reported before, this is not a unique case. A study compared the effect of low Mg intake (112mg/day) for 92 days, followed by a control period of 35 days in which the subjects were supplemented with 200 mg and kept it for 49 days. Throughout restriction phase skeletal muscle decrease significantly while serum Mg did not suffer a noteworthy reduction[29]. Dorup I et al. & Skajaa K. et al. also reported the same conclusion after comparing serum concentrations of Mg and K with

muscle-Mg and muscle-K during a diuretic treatment. They described the method of serum Mg as unreliable and unrealistic[30].

Besides muscle-Mg assessment, there is also a method considered for many authors gold standard concerning assess Mg status, which is called Mg loading test. This method consists in taking a certain quantity of Mg (oral or infusion) and after a period of 24 h its collected urine samples. This way it is possible to know how much Mg is withheld. Though this method is not practical and it is also expensive. Under certain circumstances it is described as a reliable test[31]. Although there this method is not standardized and the deficiency showed by it may not characterize the total body Mg deficit, this test has proven to be useful[32].

Red blood cell Mg is an alternative way to measure Mg status, proven to be a suitable test[29], although it has not been established as a realistic marker[28].

Apart from this, ionized Mg seems to be a good marker to evaluate Mg levels. However, Maurice J. et al writes “There appears to be no demonstrable advantage to measuring ionized Mg as opposed to total Mg for evaluating Mg status”[32].

In light of all of this Information, the best alternative for a more reliable, safe, realistic and practical way to assess Mg status, is the skeletal muscle Mg rather than serum Mg.

Ergogenic Theory

Mg takes part in many reactions in the human body, so in order to know which processes are behind the theoretical ergogenic aid, we need to identify what supplement companies claim about Mg supplementation.

Going through websites of some major supplement companies, we can find that supplementing with Mg “can” enhance the production of energy, keeps your bones strong and healthy, helps reducing weakness and fatigue, prevents cramps, contributes to normal protein synthesis, promotes a normal functioning of the brain and contributes to the normal functioning of muscles.

It is known that Mg takes part in the activation of over than 300 enzymes. Mg participates in the activation of enzymes through three major general mechanisms. By engaging in stabilization of an intermediate product, stabilizing a product leaving group and binding tow reactive substrates simultaneously and facilitating reaction through the proximity effect[33].

Mg also prevents bone fragility by destabilizing hydroxyapatite crystals, and acts synergistically with ATP to stabilize amorphous calcium phosphate and prevent hydroxyapatite formation[34].

Mg supplementation is commonly used as a solution for cramps. The mechanism behind cramps is still very unclear, but evidence points either to the lower motor neuron or its distal axonal extensions as the site of origin. The possibility of Mg supplementation suppress excitable tissue can lead us to conclude that, might also suppress muscle cramps[35].

It is claimed that Mg can reduce fatigue and weakness. In fact, there is a plausible mechanism through Mg deficiency is linked to increased inflammation and therefore to a more fatigued and weak body. This mechanism involves the priming phagocytic cells to release an inflammatory response; increasing substance P, a tachykinin neuropeptide that induces the production of proinflamatory cytokines; and activating nuclear factor-kappa ß (NFkß), a transcription factor response for the

expression of inflammation related genes. Mg deficiency leads to an increase of phagocytic cells to play their respective functions, which consequently produces reactive oxygen species[36]. The excessive production of these species will contribute to oxidative stress, affecting the surrounding tissue. Priming agents are recruited to stimulate phagocytic cells, they do not elicit oxidative stress but stimulate the production of other factors that do. Its release is induced by increased intracellular Ca^{2+}, leading to an inflammatory process. Mg deficiency could promote this increase of Ca^{2+} by activating L-type Ca channels[37]. Recent studies also indicate that the lack of Mg induces the production of proinflamatory cytokine, involving NFκβ, including TNF-α and IL-1β[37]. Mg supplementation seems to supress the production of proinflamatory cytokines whose production was increased by NFκβ. This suggest that increased levels of Ca^{2+} are responsible for Mg deficiency[37].

Mg does have an active participation in the process of protein synthesis by binding with nucleic acids. These interactions play a significant role in stabilization of the secondary and tertiary structure of DNA. Mg is essential to the cell nucleus as it is involved in the activation of enzymes important to the DNA repair, Mg is crucial for the physical integrity of double-stranded DNA[38]. Furthermore, ribonucleic acid enzymes need Mg to work as cofactor in order to be capable of recognizing and cleaving the target mRNA[39].

Mg plays a very important role in metabolic cycles, therefore supplement companies state that Mg can indeed enhance energy production. Glycolysis, Krebs cycle and β-oxidation are regulated by Mg dependent enzymes. All reactions involving ATP need the existence of Mg ions, so it can protect these molecules from

enzymatic hydrolysis. The complex Mg-ATP is crucial for catalytic activity, such as phosphotransferases, nucleotidylotransferases and ATPases[38].

Removing extracellular Mg can cause glycolysis inhibition and glucose transport limitation by the erythrocytes since many enzymes evolved in this process are Mg dependent[38]. Previous scientific trials with animals also shown a big correlation between the absence of Mg and induced alterations in glucose metabolism by compromising GLUT4 transport function, this leads to a diminish glucose absorption or assimilation in the liver or other tissues[40].

One of the most important biological processes the body of an athlete must do correctly is an efficient production of ATP. Mg has an important role in cellular respiration, Mg level in the mitochondrial matrix controls many enzymes activity like, glutamate dehydrogenase, pyruvate dehydrogenase and á-ketoglutarate[38]. Variations in the Mg flux could mean a reduction of the mitochondrial respiration rate, over more Mg seems to be an integral component of subunit IV of cytochrome c oxidase complex, which is the last enzyme of the respiratory chain responsible for oxygen reduction[38].

All these important functions can be compromised if there is a low level of Mg available for these actions, so it is essential that athletes maintain Mg within the established recommendations.

Scientific evidence

There has been a long debate whether Mg could work as an ergogenic aid or if it is just a big myth. In order to be able to recognize that Mg can be used to

improve an athlete's performance, it is necessary to analyse scientific studies capable of showing that athletes without any type of Mgdeficiency, after taking the supplement, appear to have improvements in some type of physical test compared to placebo. Although there has been a large number of studies conducted in animals which confirm the possibility that Mg can indeed better physical performance, it will not be discussed in this topic, since we are looking for evidence of enhance performance in human athletes.

Human studies concerning this matter are sparse, also the lack of a standard methodology can show some misleading results. Since almost every study conducted in humans did not use any invasive status indicator it is hard to actually know if the athletes were Mg deficient or not, even though several of them state that the subjects did not suffer from Mg deficiency.

Exercise related studies in humans can vary on which type of exercise indicator used, for that reason the studies reviewed in the monography will not contain the same type of workout indicator.

A randomized controlled trial (RCT) done with healthy elderly woman, experimented the effect of oral Mg supplementation on physical performance. Participants received a 12 week supplementation of 900mg/day of Mg oxide which actually corresponds to 300mg due to its bioavailability, then the subjects were submitted to three different exercises, and after this other tow muscle strength variables were tested (isometric knee extension torque and isokinetic and handgrip strength). When compared, the treated group only showed a greater improvement in one of the three daily exercises tested, the same results were found for the secondary outcome, meaning there were no differences between the control group and the treated once they were submitted to the strength variables. It was very clear

that the effects of the supplementation in the first outcomes were more evident in participants with intake below the RDA, which only confirms the hypothesis that Mg supplementation has beneficial effects on exercise performance in Mg deficient individuals[41].

Matias, et al. studied the impact of Mg changes on strength from a period of weight stability to a prior a competition in a sample of twenty judo male athletes who differentially reduced their level of intercellular water (ICW). Participants were divided in too groups, ICW losses below 2% and ICW losses equal to or above 2%. In the second group, it was observed a correlation between red blood cell Mg changes and handgrip maximal strength changes. This result comes to show again that adequate Mg concentrations are imperative to maintain optimal strength performance[42].

On the other hand, a study which the aim was to test the influence of Mg supplementation on physical performance in volleyball elite players (ŋ=25) indicated that a dose of 350 mg/day of Mg could enhance the performance of these players. When compared, the experimental group after the supplementation period had either a slight or significant improvement performing vertical squad jump and countermovement jump with arm swing respectively. L. Setaro et al. stated that none of the players had any kind of Mg deficiency, so the hypothesis that Mg is essential to maintain the performance in athletes with deficiency does not come into question[43].

In addition to these findings, Santos et al. trying to understand the impact of Mg intake on strength performance in elite male athletes of three different team

sports (basketball, handball, and volleyball), concluded that Mg was directly associated with muscle performance indices[44].

On the other hand, Zimmerman reviewed that Mg supplementation does not affect performance when Mg status are within normal values[45]. Moreover, a very recent review on Minerals supplementation and physical performance stated, “It has been shown that Mg supplementation may be preferable maintaining, to date there is limited evidence that Mg supplementation will improve human performance”[46].

Furthermore, a RCT tested the possible correlation between Mg supplementation and improvement of body composition and muscle strength performance in middle aged overweight women, the findings indicated that Mg supplementation did not have any significant impact on muscle strength gain[47].

Table 3. Summary of human studies.

Source	Group	Treatment	No. of participants	Age year	Main findings
Veronese et al. (2014, Italy) [41]	Elderly women	300 mg/day for 12 weeks vs control group	124	71.5 ± 5.2	Supplementation led to a positive effect on physical performance in Mg-deficient individuals
Matias et al. (2010, Portugal) [42]	Elite Judo athletes	NA	20	22.9 ± 2.9	Positive correlation between RBC and handgrip maximal strength changes
Setaro et al. (2014, Brazil) [43]	Volleyball players	350 mg/day for 4 weeks vs control group	25	17.85 ± 0.99 17.42 ± 1.56	Supplementation improved plyometric parameters countermovement jump and countermovement jump arm swing
Santos et al. (2011, Portugal) [44]	Basketball, handball, and volleyball players	NA	26	20.1 ± 4.9	Positive association between Mg intake and strength performance
Moslehi et al. (2013, Iran) [47]	Middle-aged overweight women	150 mg/day for 8 weeks vs Placebo	69	46.5 ± 3.8 46.1 ± 4.6	Supplementation had no impact on muscle strength gain in the treatment group

Discussion & Conclusion

It seems evident that Mg has an essential role in an athletes diet. What it is not so clear is if Mg supplementation when the subject has no type of deficiency can actually enhance physical performance. Several intervention studies in humans have failed in this task, only proving that Mg supplementation is beneficial when there is a clear deficiency.

Although some studies had some positive correlations between Mg and physical performance, there is always some methodological issue attach to them. For example, the methods used to evaluate Mg status are usually not the most accurate ones, masking a potential Mg deficiency. Another issue is the fact that Mg supplementation and dosages are inconsistent across different human studies. Furthermore, almost every studied reviewed had a small sample size, which could bias the statistical results.

To date, there appears to be no advantage in supplementing an athlete with Mg when it is not deficient, however it is imperative that the athlete chooses a reliable method to analyse whether or not Mg deficiency actually exists in their body.

So even more important than supplementation, it is necessary to assure that the athlete has indeed no deficit of Mg, since exercise performance may be compromised. Based upon previous studies, it is clear that an adequate nutritional intake is essential for preserving health and obtaining ideal performance in competitors and thus mineral deficiency may impair physical performance.

To summarize, this monography suggests that the real question regarding Mg supplementation is not whether or not the athlete's performance will improve,

but if the athlete is deficient in Mg or not, which in this case supplementation will make perfect sense if there is a deficit.

Also to elucidate the association of Mg supplementation and athletic performance, this monography suggests prolonged studies, with bigger samples and standardized conditions and methods, in order to acquire better and more conclusive ideas about Mg role in an athlete diet and its effect in his athletic performance.

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